PATENT COOPERATION TREATY REC'S 3 0 MAR 2005 From the INTERNATIONAL SEARCHING AUTHORITY SOMA G. SIMON GLAXOSMITHKLINE CORPORATE INTELLECTUAL PROPERTY, UW2220 WRITTEN OPINION OF THE 709 SWEDELAND ROAD, P.O. BOX 1539 INTERNATIONAL SEARCHING AUTHORITY KING OF PRUSSIA, PA 19406-0939 (PCT Rule 43bis.1) Date of mailing 28 MAR 2005 (day/month/year) FOR FURTHER ACTION Applicant's or agent's file reference See paragraph 2 below PU60293 International filing date (day/month/year) Priority date (day/month/year) International application No. 06 June 2003 (06.06.2003) 04 June 2004 (04.06.2004) PCT/US04/17892 International Patent Classification (IPC) or both national classification and IPC IPC(7): C07D 285/30; A61K 31/5415 and US Cl.: 544/47; 514/223.2 Applicant SMITHKLINE BEECHAM CORPORATION 1. This opinion contains indications relating to the following items: Box No. I Basis of the opinion Box No. II Priority Non-establishment of opinion with regard to novelty, inventive step and industrial applicability Box No. III Lack of unity of invention Box No. IV Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial Box No. V applicability; citations and explanations supporting such statement Certain documents cited Box No. VI Certain defects in the international application Box No. VII Certain observations on the international application Box No. VIII 2. FURTHER ACTION If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered. If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. For further options, see Form PCT/ISA/220. 3. For further details, see notes to Form PCT/ISA/220. Authorized officer Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US James Wilson Commissioner for Patents P.O. Box 1450

Telephone No. 571-272-0661

Alexandria, Virginia 22313-1450

Form PCT/ISA/237 (cover sheet) (January 2004)

Facsimile No. (703) 305-3230

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/17892

| | Box No. I Basis of this opinion | | |
|------------|--|--|--|
| | 1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item. This opinion has been established on the basis of a translation from the original language into the following language which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)). 2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of: a. type of material a sequence listing | | |
| <i>)</i> * | table(s) related to the sequence listing b. format of material in written format in computer readable form | | |
| | c. time of filing/furnishing contained in international application as filed. filed together with the international application in computer readable form. furnished subsequently to this Authority for the purposes of search. | | |
|) | In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished. Additional comments: | | |
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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/US04/17892

| applicability; citations and expl | e 43 bis.1(a)(i) with regard to novelty, inven- anations supporting such statement | |
|--|--|----------------------------------|
| Novelty (N) | Claims 1-4 Claims NONE | YES |
| Inventive step (IS) | Claims 1-4 Claims NONE | YES NO |
| Industrial applicability (IA) | Claims 1-4 Claims NONE | YES |
| Claims 1-4 meet the criteria set out in PCT Article such as phenyl and cyclopentyl attached to the ber | 2 33(2)-(3), because the prior art does not teach or for a standard transfer of the standard tra | airly suggest a carbocyclic ring |

Claims 1-4 meet the criteria set out in PCT Article 33(4), and thus the 1,2,4-benzothiadiazin-5-ol compounds can be used in the manufacture of a medicine for therapeutic treatment of a disease state in a human or other mammal, which is exacerbated or caused by unregulated IL-8 cytokine production by such mammal's cell, because the subject matter claimed can be made or used in industry.

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